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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/010,914	12/05/2001	Shanker Gupta	9022.30	6114

20792 7590 07/28/2004

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EXAMINER	
CHOI, FRANK I	

ART UNIT	PAPER NUMBER
1616	

DATE MAILED: 07/28/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/010,914	GUPTA ET AL.	
	Examiner	Art Unit	
	Frank I Choi	1616	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *02 April 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *11-41* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *11-41* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 4/2/2004 has been entered.

Specification

Pg. 10, lines 13,14, please update reference to the cited application by indicating that it is now Patent No. 6,368,831.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 11-41 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. The Specification only discloses egg phospholipids in the context of being a non-ionic surfactant. As such, according to the Specification the egg phospholipid would have to be non-ionic. However, as indicated previously in the prior Office Actions, in the context of an enablement rejection, the specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention

commensurate in scope with these claims. Applicant lists egg phospholipids as non-ionic surfactants, however, the prior art cited indicates that egg phospholipids are ionic surfactants. Applicant does not appear to show how the egg phospholipids are nonionic, as such, it appears that a skilled artisan would be required to do undue experimentation in order to make and/or use a non-ionic egg phospholipid. Since non-ionic egg phospholipids are non-enabled and Applicant does not describe the use of other forms of egg phospholipids other than non-ionic, Applicant's insertion of egg phospholipids per se constitutes new matter.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 11-41 are rejected under 35 U.S.C. 103(a) as being unpatentable over Lopez-Berestein et al. (US 2002/0143062) in view of Chen et al. (US 6,267,985) and Shudo et al. (US 5,676,146).

Lopez-Berestein et al. teach a method of preparing a liposome by combining N-(4-hydroxyphenyl) retinamide with a phosphatidylcholine, soybean oil, alcohol and water and that typically that liposome are delivered in injectable compositions (Pg. 28, paragraphs 0030,0331, Pg. 29, Paragraph 0340). It is taught that the phosphatidylcholine can be a egg phosphatidyl choline (Pg. 10, Paragraphs 0081,0089). It is taught that the parenteral aqueous solution should be suitably buffered, if necessary and rendered isotonic (Pg. 29, paragraph 0334). It is taught that retinoids are suitable for the treatment of cancer (Pg. 1, paragraph 0010). It is taught that

said retinamide associated with a lipid may emulsified with a lipid or form a liposome as indicated above (Page 10, Paragraphs 0091, Page 11, Paragraphs 0091, 0092). It is taught that methods for preparing lipid emulsions and adding additional components are well known in the art (Page 11, paragraphs 0094, 0095).

Chen et al. teach that the addition of triglcyerides, such as soybean oil, are conventionally used to increase the solubility of many therapeutic agents (Column 1, lines 10-27, Column 6, lines 17). It is taught that the solubilizers such as ethanol can be added increase the solubility of the therapeutic agent or triglyceride in the composition (Column 33, lines 62-68, Column 34, lines 1-33). It is taught that small particle sizes avoid safety problems found with large particle sizes in parenteral administration (Column 40, lines 26-35). The use of surfactants such as PEG fatty acid esters and POE-POP box copolymers are is taught (Columns 9, 10, Column 20, lines 54-68).

Shudo et al. teach that glycerine is used pharmaceutical formulations for injection as an isotonizing agent (Column 5, lines 47-55).

The difference between the prior art and the claimed invention is that the prior art does not expressly disclose the retinide composition having the claimed components in the claimed amounts. However, the prior art amply suggests the same as the prior art teaches the used of emulsions to administer hydrophobic drugs, including retinoids, for the treatment of cancer, in the form of emulsions. Further, it would have well within the skill of and one of ordinary skill in the art would have been motivated to use a lipid, such as soy bean oil, with the expectation of increasing the solubility of the retinoid, a solvent such as ethanol with the expectation of increasing the solubility of the retinoid and/or lipid, a non-ionic surfactant with the expectation

of increasing the ability of the triglyceride to solubilize the retinide. Further, it would have been well within the skill of one of ordinary skill in the art to use various amounts of the components, including amounts falling within the claimed amounts, depending on the amount of drug, ph, tonicity, stability, solubility and clarity desired.

Examiner has duly considered Applicant's arguments but deems them unpersuasive.

Applicant argues that tertiarybutyl alcohol is toxic to humans, however, Applicant does not provide any evidence that tertiary butyl alcohol as used in Lopez-Berestein reference will be toxic to humans. Further, the claims do not exclude the use of use of tertiary butyl alcohol. The mere fact (Examiner notes that Applicant has provided no evidence of the same) that FDA approval is low with respect to liposomes is not sufficient to overcome the rejection herein as FDA approval is not a prerequisite for determining the obviousness or non-obviousness of the present claims. There is nothing in Lopez-Berestein et al.which indicates a failure to formulate fenretinide in a more easily manufactured and quality-controllable composition, as Lopez-Berestein et al. clearly indicates that emulsions are well within the skill of one of ordinary skill in the art. Applicant does not indicate how Chen et al.or Shudo et al. fail to teach or provide the missing elements of Lopez-Berestein et al. or for that matter what the missing elements are in Lopez-Berestein et al. Applicant has made no showing the limitation "consisting essentially of" excludes tertiary butyl alcohol. Further, Lopez-Berestein et al. does not require the use of tertiary butyl alcohol to prepare the liposomes (See paragraphs 0103-0108).

Therefore, the claimed invention, as a whole, would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, because every element of the invention has been collectively taught by the combined teachings of the references.

Conclusion

A facsimile center has been established in Technology Center 1600. The hours of operation are Monday through Friday, 8:45 AM to 4:45 PM. The telecopier number for accessing the facsimile machine is (703) 872-9306.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Frank Choi whose telephone number is (571)272-0610. Examiner maintains a flexible schedule. However, Examiner may generally be reached Monday-Friday, 8:00 am – 5:30 pm (EST), except the first Friday of the each biweek which is Examiner's normally scheduled day off.

If attempts to reach the Examiner by telephone are unsuccessful, the Examiner's Supervisor, Mr. Gary Kunz, can be reached at 571-272-0887. Additionally, Technology Center 1600's Receptionist and Customer Service can be reached at (571) 272-1600.

FIC
July 26, 2004

NEIL S. LEVY
PRIMARY EXAMINER